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Supervised Exercise Training for Intermittent Claudication: Lasting Benefit at Three Years

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Objectives. *To assess the long-term outcome of supervised exercise training for intermittent claudication.*
Methods. *A prospective study was undertaken of all patients referred to a single centre with intermittent claudication (>46 m). Patients underwent supervised exercise training twice weekly for 10 weeks, with regular follow-up to 3 years. Actual Claudication Distance (ACD), Maximum Walking Distance (MWD) and ankle-brachial pressure indices (ABPI) were measured.*
Results. *In 202 patients the initial median ACD and MWD were 112 m and 197 m. Following exercise therapy both the median ACD and MWD increased to 266 m and 477 m at three months, increases of 237% and 242% respectively ($p < 0.001$). At three years the median ACD and MWD were 250 m and 372 m, increases of 223% and 188% respectively ($p < 0.001$). There was no significant change in ACD or MWD at 3 months compared to 1, 2 or 3 years. ABPI remained unchanged throughout.*
Conclusions. *Supervised exercise training has long term benefit in patients with intermittent claudication. Results seen at 12 weeks are sustained at three years.*

Keywords: Vascular; Claudication; Exercise; Supervised.

Introduction

Peripheral vascular disease (PVD) is common, affecting 20% of people over 70 years, and is a manifestation of systemic atherosclerosis. Symptoms of intermittent claudication are present in 15–40% patients.[1,2] Although PVD causes disability and reduction in quality of life, the natural history in the affected limb is relatively benign. Only 25% patients show symptomatic deterioration and approximately 2% progress to amputation.[3] There is, however, a high associated cardiovascular risk, particularly of myocardial infarction and stroke. 50% of claudicants die within 10 years, a relative risk of 3.8 compared with the normal population.[4]

Treatment of claudication is initially conservative with control of risk factors and medical therapy. Exercise as a treatment for intermittent claudication has shown benefit in several small trials.[5,6] A meta-analysis of randomised and non-randomised trials showed that exercise programmes improve symptoms in patients with claudication, with a 180% increase in distance to onset of claudication pain and a 120% increase in maximum walking distance.[5] The greatest improvement occurred when patients exercised by walking to near-maximal pain in sessions of greater than 30 minutes each, at least three times a week, for more than six months. A Cochrane review of randomised trials of exercise for intermittent claudication had similar findings with a 150% mean improvement in maximal walking distance. They commented that data was predominantly from small trials with an average of 25 patients and short follow-up.[7] Consequently concern exists that the benefit seen from exercise training may be temporary, as little long term follow up data exists. The aim of this prospective study is to assess the long-term efficacy of supervised exercise training for intermittent claudication.

Methods

Patient recruitment

This study was undertaken at the vascular unit in a large district general hospital, where three vascular

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surgeons serve a population of 350,000. Patients attending the vascular service for whom intermittent claudication was the main factor affecting mobility were considered. Data was collected prospectively on patients with intermittent claudication who had been entered into a supervised exercise programme from 1999–2004.

Inclusion criteria

The diagnosis of intermittent claudication was made on the history, clinical examination and measurement of ankle-brachial pressure indices (ABPI) before and after exercise.[8] All patients had a resting ABPI < 0.9 and a positive response to a validated stress test (a drop in ankle pressure of >30 mmHg following 2 minutes of treadmill walking at 10% incline and 3.2 km/h measured 40 sec post exercise[9]). If any doubt existed a Duplex ultrasound scan was performed. All patients had stable intermittent claudication for a minimum of 3 months and were able to walk >300 m on the flat in 6 minutes.

After diagnosis risk factor modification and options for treatment were discussed with each patient. The normal protocol was that patients with mild to moderate intermittent claudication (Fontaine Stage II[3]) were referred for exercise therapy. Patients who wished to have further investigation with a view to interventional treatment had an arterial Duplex scan carried out and were offered angioplasty as appropriate. Patients who were not suitable for angioplasty were referred for exercise therapy. All patients who underwent exercise therapy were included for analysis.

Exclusion criteria

All patients with severe claudication who were unable to walk more than 46 metres (50 yards) were routinely considered for further intervention by angioplasty or reconstructive surgery and were excluded. In addition the following patients were excluded: those who had suffered a myocardial infarction, unstable angina or cerebrovascular accident or undergone major surgery in the previous three months, and patients with significant comorbidity preventing participation in an exercise programme.

Outcome measures

A walk test was carried out to measure the Actual Claudication Distance (ACD) and Maximum Walking Distance (MWD). ACD was defined as the distance walked until the patient experienced the onset of muscle pain. MWD was defined as the maximum distance a patient could walk until they had to stop. At the start of the programme the ACD and MWD were measured by the distance walked along a corridor, following the purchase of a treadmill all walk tests were and on a treadmill at a fixed speed (3.2 km/h on the flat).

Exercise class

Supervised exercise training comprised of two classes a week, each lasting one hour, for ten weeks, supervised by a vascular nurse specialist and senior physiotherapist. Each class started with undirected cycling on a static bike for 5 minutes, followed by stretching exercises as a warm-up. Formal exercises were then performed, comprising of heel raises, step-ups and sit to stand, each in repetitions of ten. Patients exercised again on the static bike (no set speed or resistance for 5–10 min) and walked on the treadmill (3.2 km/h for up to 15 min). This was initially on the flat. Patients were subsequently encouraged to walk on an increasing incline up to a maximum of 10% as their walking ability improved, this was individually tailored over time.

Patients were exercised to near maximal pain in each exercise as determined by a visual analogue pain scale, and then rested until pain-free before starting the next one. Each patient kept an individual record of progress and perception of pain. As walking ability improved the intensity of training was increased for each individual by increasing the repetition of each exercise.

Whilst attending the programme patients were advised to exercise at home on the days that they were not attending the classes and encouraged to take daily walks, exercising beyond the onset of claudication. After completing the programme all patients were followed up by the vascular nurse specialist at 3, 6, 12, 24 and 36 months with a repeat walk test and ABPI. Each patient's consultant and general practitioner were informed of progress by letter. Appropriate patients were advised of the 'Fit for the Future' Programme involving local leisure centres with reduced joining fees.

Some patients obtained sufficient benefit from supervised exercise training that they were able to walk more than ten minutes on the treadmill (to a total distance of 570 m) without symptoms (see Table 1). They were discharged from follow-up, essentially pain-free. A distance of 570 m was recorded for analysis at this time point.

Endpoints

Primary endpoints for analysis were differences in ACD, MWD and ABPI at 3, 6, 12, 24 and 36 months.

Table 1. Outcome of patients undergoing supervised exercise therapy for intermittent claudication at 3, 6, 12, 24 and 36 months

Outcome	3	6	12	24	36
Walk test	199	171	142	87	60
Discharged		1	2	10	21
Did not attend	3	4	5	0	2
Died		3	6	10	12
Operation		1	3	6	9
Outpatient appointment			3	3	3
Medically discharged		1	3	6	7
MIMIC Trial		1	1	3	3
Lost to follow-up		7	8	13	13
Total	202	189	173	138	130

Outcomes were: underwent walk test, discharged able to walk without symptoms, failed to attend, died, underwent operation, awaiting outpatient appointment to discuss treatment options, discharged unable to exercise for medical reasons, enrolled in further trial (MIMIC) and lost to follow-up.

Secondary endpoints for analysis were the need for intervention (angioplasty or surgery), death or discharge for medical reasons. The data was analysed using Instat 3 (www.graphpad.com).

Results

202 patients completed supervised exercise training. Their average age was 68 years (range 40–89) and 151 (75%) were male. Patient risk factors included smoking (47 current, 81 ex-smokers), hypertension (93), high cholesterol (77) and diabetes (37). At initial assessment the median ACD was 112 m (IQR 82–168) and median MWD 197 m (IQR 47–357). Although the walk test was initially performed by corridor walk ($n = 32$, 16%) and subsequently by treadmill ($n = 170$, 84%), there was no significant difference in ACD or MWD as assessed by either method, either at initial assessment (ACD $p = 0.17$, MWD $p = 0.34$) or subsequent follow-up at any time point. The average ABPI at initial assessment was 0.64 (s.d. 0.18).

At three months following exercise therapy the median ACD increased to 266 m (IQR 160–483, $p < 0.001$) and the median MWD increased to 477 m (IQR 280–570, $p < 0.001$), increases of 237% and 242% respectively. More than 90% of patients benefited from exercise therapy with an individual increase in their ACD and MWD (Table 2). At 6, 12, 24 and 36 months both ACD and MWD remained increased compared to initial assessment and unchanged from 3 months (non-parametric ANOVA $p < 0.001$, Figs. 1, 2). At 36 months the median ACD was 250 m (IQR 152–446) and the median MWD 372 m (IQR 224–840), increases of 223% and 188% respectively over values at the initial assessment. There was no difference between results seen at 3, 6, 12, 24 and 36 months for ACD or MWD (non-parametric ANOVA $p < 0.001$, with Dunn's multiple comparison test $p > 0.05$).

Table 2. Benefit following exercise therapy at 3 and 36 months

	3 months ($n = 199$)		36 months ($n = 81$)	
	ACD	MWD	ACD	MWD
Benefit	185 (93%)	182 (91%)	77 (95%)	72 (89%)
Worse	14 (7%)	17 (9%)	4 (5%)	9 (11%)

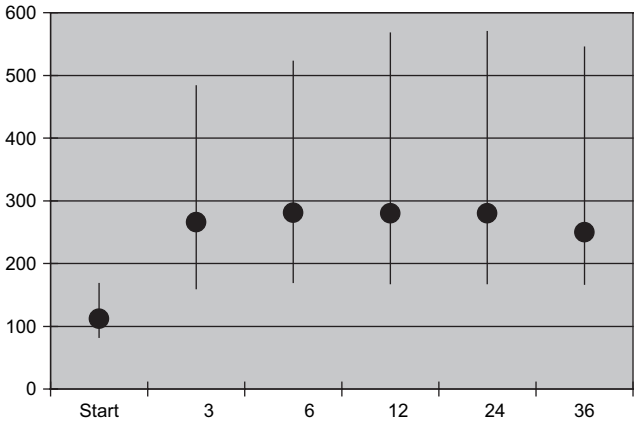

Fig. 1. Actual Claudication distance (metres) at the start and 3, 6, 12, 24 and 36 months following exercise therapy. Data are presented as medians and interquartile ranges.

The mean resting ABPI remained unchanged throughout the study at 0.64 at 3 months and 1 year, and 0.61 at 3 years (N.S., Fig. 3).

At three years 130 patients were available for analysis, the remainder were still in follow up at different time points. Sixty patients were still under annual review and underwent a walk test. A further 21 had been discharged, able to walk pain free more than

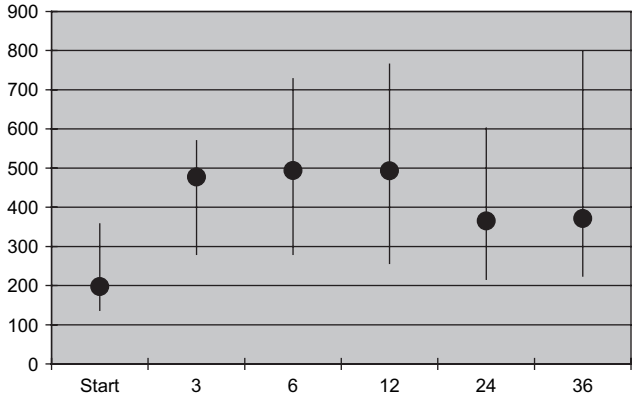

Fig. 2. Maximum Walking Distance (metres) at the start and 3, 6, 12, 24 and 36 months following exercise therapy. Data are presented as medians and interquartile ranges.

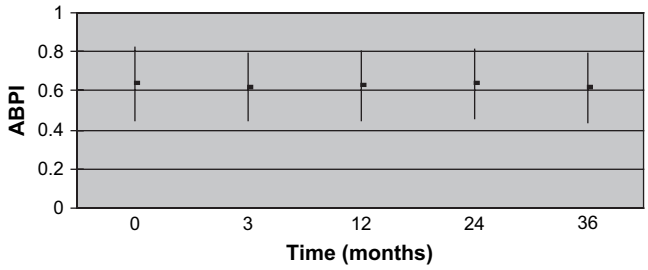

Fig. 3. Resting Ankle-Brachial Pressure Index (ABPI) after recruitment into supervised exercise programme. Data are presented as means and standard deviations.

570 m. Of these 81 patients, most had continued improvement in their ACD and MWD (Table 2). Nine (6.9%) had undergone vascular intervention (5 bypass surgery, 4 angioplasty) with one (0.8%) amputation, and twelve (9.2%) patients had died (5 ischaemic heart disease, 2 carcinoma bronchus, 1 multiple hepatic metastases, 1 cerebrovascular accident, 3 cause unknown). Seven were medically discharged unable to continue walking for other reasons (4 with cardiac problems and one each with bronchiectasis, carcinoma of stomach and stroke). The outcome of patients at each time point is listed in Table 1.

Discussion

The results of this study add strong support to the evidence that supervised exercise is of symptomatic benefit for intermittent claudication.

A meta-analysis showed that the greatest improvement occurred when patients exercised at least three times a week for more than six months,[5] compared with twice a week for 10 weeks in this study. Our exercise programme started in 1998, at a time when few exercise programmes were in existence in the UK and none of these to our knowledge had a frequency of three times per week. The frequency of twice weekly classes was chosen and based on the successful results obtained with this approach by the Oxford group.[6,10] It was also found to be practical and well accepted by patients.

All patients in this study were also advised to exercise at home on the days that they were not attending the classes and encouraged to take daily walks, exercising beyond the onset of claudication. After completion of the exercise programme a vascular nurse specialist followed up all patients annually. Although we did not document the exercise regimens of individual patients during follow up, many patients reported having a set walk they undertook daily or having bought an exercise bike or treadmill. Many patients regarded the annual follow up appointment as a challenge. The role of continued support and encouragement at follow up are likely to be important contributory factors to these results.

At the start of the study 24% patients were smokers, and all patients were encouraged to stop smoking completely if possible. Unfortunately we did not collect data on the effect of smoking cessation and walking distance, partly because this would have involved additional measurement of smoke markers[11] and this would have further complicated the study. However these results would still show a significant benefit from exercise therapy, even if all 47 smokers had stopped smoking completely, which is most unlikely.

After the initial dramatic in walking ability at 3 months up to 1 year there was no further significant improvement at 2 and 3 years, but the increase was sustained. At 3 years patients were able to walk twice as far on average before their claudication pain developed, and also before they had to stop walking. This is in contrast to other studies in which walking ability reduced and a partial loss of training effect occurred, after initial improvement.[12]

In the Cochrane review, 10 trials and a total of almost 250 patients were analysed.[7] These were all small (25–49) patients and follow-up ranged from 12 weeks to 15 months. There was some variation in the exercise regimens used, although all recommended at least two weekly sessions of mostly supervised exercise. It was concluded that a thrice-weekly regimen of walking to near-maximal pain provides the best improvement. The data presented here show that improvement in walking ability was obtained in twice weekly sessions. Our exercise therapy was supervised for 10 weeks and suggests that there may be no need for longer courses of more than 6 months, as has been suggested.[5]

It is clear that the previous standard advice of a decade and more ago to ''stop smoking and keep walking''[13] should be replaced by a structured and coordinated plan of care involving routine access to supervised exercise programmes. These should be made available to all affected patients. In these data we did not assess quality of life before and after exercise therapy. Cheetham found that supervised exercise provides a significant improvement in patients' symptoms and quality of life compared with advice alone,[14] and there is little evidence that exercise advice alone is effective treatment.[15]

The mechanisms behind the improvement in walking ability are multifactorial and include a redistribution of blood flow, changes in oxidative capacity of the skeletal muscles and greater utilisiation of oxygen, together with improved blood rheology and decreased

injurious effects of exercise-induced ischaemia-reperfusion injury.[16–18] The relative importance of these factors is uncertain, but it is clear that the response to supervised exercise training occurs quickly with a maximal effect at 3 months from commencement. We should now be able to give this positive message to patients with intermittent claudication. Not only should affected patients expect to be entered into a supervised exercise programme, they can also expect a rapid and marked improvement in their symptoms with this safe and simple therapy and changes to their life style, with lasting benefit.

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